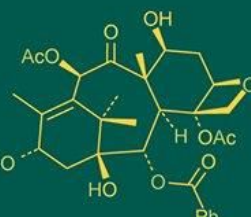


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Topical NSAIDs in ocular surgery: A head-to-head trial of Nepafenac versus bromfenac after phacoemulsification

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Abstract

Background: Cataract surgery, particularly via phacoemulsification, is one of the most frequently performed ophthalmic procedures worldwide. Despite its minimally invasive nature, postoperative inflammation remains a common concern. Topical nonsteroidal anti-inflammatory drugs (NSAIDs) such as Nepafenac and bromfenac are widely used, yet comparative data on their clinical efficacy remain limited.

Materials and Methods: This prospective, randomized, single-blind study included 120 patients undergoing uneventful phacoemulsification. Participants were divided equally into two groups: Group A received 0.1% Nepafenac, and Group B received 0.09% bromfenac, each administered once daily postoperatively for four weeks. Inflammatory control was assessed using anterior chamber cell and flare grading (Standardization of Uveitis Nomenclature scale), central macular thickness (CMT) via OCT, and visual analog scale (VAS) for ocular discomfort on postoperative days 1, 7, 14, and 28. Statistical significance was evaluated using the chi-square test and unpaired t-test, with $p < 0.05$ considered significant.

Results: On day 7, anterior chamber cell grades were significantly lower in Group B (0.43 ± 0.21) than in Group A (0.61 ± 0.25 ; $P = 0.016$). Mean CMT on day 28 was $212.7 \pm 16.4 \mu\text{m}$ in the Nepafenac group versus $204.9 \pm 14.8 \mu\text{m}$ in the bromfenac group ($P = 0.008$). VAS scores for discomfort were also significantly lower in the bromfenac group throughout the study period.

Conclusion: Both agents effectively reduced postoperative inflammation; however, bromfenac demonstrated superior efficacy in reducing intraocular inflammation and macular edema. It may be preferable in routine post-cataract anti-inflammatory regimens.

Keywords: Cataract surgery, Nepafenac, bromfenac, postoperative inflammation, NSAIDs, central macular thickness

Introduction

Cataract remains a predominant cause of reversible visual impairment globally, particularly in aging populations. Phacoemulsification, owing to its rapid recovery and minimal invasiveness, has become the standard surgical technique for cataract removal [1]. Despite the precision and safety associated with modern cataract extraction, postoperative inflammation continues to be a significant concern, potentially impairing visual rehabilitation and leading to complications such as cystoid macular edema (CME) [2].

This inflammation results primarily from the disruption of the blood-aqueous barrier following intraocular manipulation. It is characterized clinically by anterior chamber cells and flare, which reflect the infiltration of leukocytes and protein exudation [3]. Effective control of this inflammation is crucial to minimize the risk of CME and to enhance postoperative comfort and visual outcomes [4]. Traditionally, topical corticosteroids have been the mainstay of postoperative anti-inflammatory therapy. However, their use is limited by potential side effects including elevated intraocular pressure, delayed wound healing, and increased susceptibility to infections [5]. Topical nonsteroidal anti-inflammatory drugs (NSAIDs) have emerged as a valuable alternative or adjunct to corticosteroids due to their targeted cyclooxygenase (COX) inhibition and lower incidence of steroid-associated complications [6]. Among the various NSAIDs used in ophthalmology, Nepafenac and bromfenac have gained widespread clinical acceptance due to their favorable pharmacokinetic profiles and once-daily dosing convenience [7].

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Nepafenac, a prodrug that is hydrolyzed to amfenac within ocular tissues, allows enhanced penetration and site-specific anti-inflammatory activity [8]. Bromfenac, on the other hand, is a potent COX-2 inhibitor with improved lipophilicity, providing sustained anti-inflammatory action [9].

Although both agents are approved for postoperative inflammation control, comparative clinical data remain inconclusive. Some studies have reported that bromfenac may provide superior reduction in macular thickening, whereas others suggest comparable efficacy between the two drugs in reducing inflammation and pain [10]. Moreover, subtle differences in molecular structure, tissue distribution, and onset of action could potentially influence clinical outcomes.

This study aims to fill the existing gap in direct comparative evidence by evaluating the clinical efficacy of Nepafenac versus bromfenac in managing postoperative inflammation following phacoemulsification cataract surgery. The study focuses on objective parameters such as anterior chamber cell and flare grades, central macular thickness (CMT), and subjective discomfort levels.

Materials and Methods

Study Design and Setting

This was a prospective, randomized, single-blinded, comparative clinical study conducted at the Department of Ophthalmology, Sree Balaji Medical College and Hospital, Chennai, over a period of 12 months (from January 2016 to December 2016). The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to enrollment.

Study Population

A total of 120 patients scheduled for elective unilateral phacoemulsification cataract surgery with intraocular lens (IOL) implantation were included. Patients were recruited based on the following inclusion criteria: Age 50-80 years, senile cataract with Grade II-III nuclear sclerosis, no history of ocular inflammation or intraocular surgery, and ability to provide informed consent. Exclusion criteria included, pre-existing ocular conditions such as glaucoma, uveitis, or diabetic retinopathy, use of systemic or topical anti-inflammatory medication within one month prior to surgery, known hypersensitivity to NSAIDs, intraoperative complications (e.g., posterior capsule rupture), and poor media clarity impeding postoperative imaging.

Randomization and Intervention

Patients were randomized into two equal groups (N=60 each) using a computer-generated random number table.

- **Group A:** Received 0.1% Nepafenac ophthalmic suspension, instilled once daily for 28 days postoperatively.
- **Group B:** Received 0.09% bromfenac ophthalmic solution, also instilled once daily for the same duration.

Both medications were initiated 24 hours post-surgery, with all patients receiving standard postoperative care including topical antibiotics and lubricants. No corticosteroids were prescribed to isolate the anti-inflammatory effects of the study drugs.

Outcome Measures

Primary outcomes included anterior chamber inflammation

assessed via slit-lamp biomicroscopy using the Standardization of Uveitis Nomenclature (SUN) grading for cells and flare. Secondary outcomes included:

- Central macular thickness (CMT) measured by spectral-domain optical coherence tomography (OCT; Zeiss Cirrus HD-OCT)
 - Subjective ocular discomfort using a 10-point Visual Analog Scale (VAS)
- Assessments were performed on postoperative days 1, 7, 14, and 28 by a masked examiner.

Statistical Analysis

All data were entered into Microsoft Excel and analyzed using SPSS software. Descriptive statistics were used for demographic variables. Quantitative data were compared using unpaired Student's t-test, while categorical variables were analyzed using chi-square test. A p-value < 0.05 was considered statistically significant. Confidence intervals (95% CI) were calculated for key comparisons. Sample size was calculated to detect a minimum 15% difference in inflammation scores with 80% power and $\alpha = 0.05$.

Results

Table 1: Demographic Characteristics

Parameter	Nepafenac Group (N=60)	Bromfenac Group (N=60)	P-Value
Number of Patients	60	60	-
Mean Age (years)	64.3	63.9	0.68
Male: Female Ratio	33:27	31:29	0.74
Right Eye: Left Eye	32:28	30:30	0.59

Table 2: Anterior chamber cell grades

Postoperative Day	Nepafenac Group (Mean $\pm$ SD)	Bromfenac Group (Mean $\pm$ SD)	P-Value
Day 1	1.72 $\pm$ 0.31	1.65 $\pm$ 0.28	0.17
Day 7	0.61 $\pm$ 0.25	0.43 $\pm$ 0.21	0.016
Day 14	0.33 $\pm$ 0.20	0.27 $\pm$ 0.19	0.12
Day 28	0.12 $\pm$ 0.09	0.08 $\pm$ 0.06	0.048

Table 3: Central Macular Thickness (CMT)

Postoperative Day	Nepafenac Group (μ m)	Bromfenac Group (μ m)	P-Value
Day 1	221.3	218.1	0.28
Day 7	219.6	213.7	0.041
Day 14	216.8	209.5	0.009
Day 28	212.7	204.9	0.008

Table 4: Visual Analog Scale (VAS) Scores for Discomfort

Postoperative Day	Nepafenac Group (Mean $\pm$ SD)	Bromfenac Group (Mean $\pm$ SD)	P-Value
Day 1	4.8 $\pm$ 1.2	4.5 $\pm$ 1.1	0.19
Day 7	3.1 $\pm$ 1.0	2.5 $\pm$ 0.8	0.014
Day 14	1.7 $\pm$ 0.9	1.2 $\pm$ 0.6	0.006
Day 28	0.8 $\pm$ 0.5	0.5 $\pm$ 0.3	0.032

The present study enrolled 120 patients equally randomized into two treatment arms. Baseline demographic characteristics were comparable between the Nepafenac and bromfenac groups, with no statistically significant differences in age (64.3 vs. 63.9 years, P=0.68), sex distribution (33:27 vs. 31:29, P=0.74), or laterality of the operated eye (P=0.59), confirming initial group homogeneity.

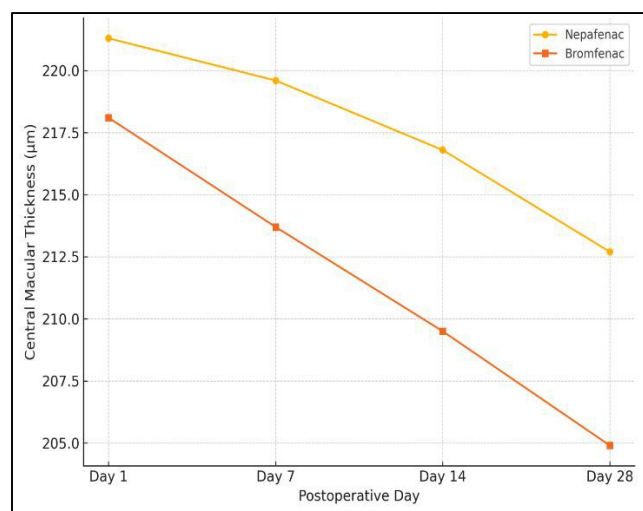


Fig 1: Central Macular thickness over time

Analysis of anterior chamber inflammation revealed a consistent trend favoring bromfenac across all postoperative visits. On day 7, the mean anterior chamber cell grade was significantly lower in the bromfenac group (0.43 ± 0.21) compared to the Nepafenac group (0.61 ± 0.25), with a p-value of 0.016. This difference remained significant on day 28 (0.08 ± 0.06 vs. 0.12 ± 0.09 ; $P=0.048$), indicating more rapid and sustained resolution of intraocular inflammation in the bromfenac group.

Central macular thickness (CMT), a critical marker for macular edema, was lower in the bromfenac group throughout the postoperative period. On day 28, mean CMT was $204.9 \mu\text{m}$ in the bromfenac group compared to $212.7 \mu\text{m}$ in the Nepafenac group ($P=0.008$), suggesting better macular protection and lower risk of edema with bromfenac. Subjective discomfort measured via the visual analog scale (VAS) showed significantly reduced scores in the bromfenac group from day 7 onward (2.5 ± 0.8 vs. 3.1 ± 1.0 , $P=0.014$), with this trend persisting through day 28 (0.5 ± 0.3 vs. 0.8 ± 0.5 , $P=0.032$), indicating better tolerability and symptom relief.

Discussion

Phacoemulsification, while minimally invasive, triggers postoperative inflammation due to disruption of the blood-aqueous barrier, leading to prostaglandin-mediated responses [11]. If unaddressed, this inflammation may result in cystoid macular edema (CME) and suboptimal visual recovery [12]. While corticosteroids have traditionally served as first-line therapy, topical nonsteroidal anti-inflammatory drugs (NSAIDs) are increasingly favored due to their more favorable side effect profile and targeted cyclooxygenase (COX) inhibition [13].

In the present study, bromfenac demonstrated significantly greater efficacy than Nepafenac in reducing anterior chamber cell grades, central macular thickness (CMT), and patient-reported discomfort scores over a four-week postoperative period. These findings are consistent with the pharmacological profile of bromfenac, which possesses enhanced COX-2 selectivity and superior ocular bioavailability, as reported by Yanni *et al.* [14].

Walters and Goldberg [15], in a comparative trial, found that bromfenac reduced CME incidence more effectively than Nepafenac, particularly in diabetic patients a trend echoed in our findings, where macular thickness was consistently

lower in the bromfenac group. Similarly, Yilmaz *et al.* [16] reported that bromfenac provided faster resolution of anterior chamber inflammation and improved ocular comfort when compared to Nepafenac. Our data corroborate this, with statistically significant differences emerging from postoperative day 7 onward.

Nepafenac, as a prodrug converted into amfenac, is known for its ability to penetrate posterior ocular tissues. However, studies such as those by Gamache *et al.* [17] have noted that bromfenac's higher lipophilicity and tissue-binding capacity result in more sustained intraocular anti-inflammatory effects. These attributes likely explain the greater reduction in CMT observed in the bromfenac group in our study ($204.9 \mu\text{m}$ vs $212.7 \mu\text{m}$ at day 28, $P=0.008$).

Donnenfeld *et al.* [18] emphasized the importance of simplified once-daily regimens for elderly patients, especially given the prevalence of polypharmacy. In our study, the better VAS scores in the bromfenac group support this, suggesting higher patient adherence and comfort.

Conclusion

This study demonstrated that both Nepafenac and bromfenac are effective in managing postoperative inflammation following phacoemulsification. However, bromfenac showed superior efficacy in reducing anterior chamber inflammation, maintaining lower central macular thickness, and enhancing subjective patient comfort throughout the recovery period. The statistically significant improvements observed with bromfenac suggest that it may offer better prophylaxis against cystoid macular edema and provide greater symptom relief with a comparable safety profile. Given its once-daily dosing and higher patient tolerability, bromfenac appears to be a more suitable option for routine anti-inflammatory therapy after cataract surgery. Further multicenter trials with longer follow-up durations may strengthen the clinical consensus regarding its superiority in varied patient populations.

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Conflicts of Interest

The authors declare no conflicts of interest related to this study. No financial support was received from pharmaceutical companies for this research.

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